Open questions

The good fairy godmother of science

Lewis Wolpert

There is a story that Einstein did not pursue a career in mathematics, not because he was not good enough, but because he did not have the 'nose' for recognizing the important problems. It is just as creative to define scientific problems as it is to solve them. As Peter Medawar put it, "Science is the Art of the Soluble". So the trick is to define those problems that can be solved and to know what questions to ask. A fundamental change in biology occurred, for example, when the questions about proteins changed from asking where the energy to synthesize them comes from, to where the information comes from for putting the amino acids in the right order. Of course, this required Sanger's discovery that there is a right order.

With the powerful techniques of molecular biology, genetics, electrophysiology, imaging and so on that are available today, there may be a tendency for science to be technology-driven: the techniques dictate the next experiment. This is not necessarily a bad thing. In my own field, developmental biology, I have argued that the principles are understood and all that remains is to fill in the details of how the thousands of genes controlling development work [1]. But am I correct? Perhaps there are many new principles to be discovered and I have not framed the questions correctly.

But the more general issue is: what are the really interesting questions in biology that need to be answered? If the good fairy godmother of science (GOOFGOOS) allowed one to ask just one question to which she would give the correct answer, what would one ask? There are limitations — one cannot ask a very general question, such as: how does the brain work? It has to be more specific, and should be answerable in no more than 30 words. The nice thing about asking the GOOFGOOS is that she does not demand that we know how to solve the problem, or have the techniques to do it.

The question I would like to ask the GOOFGOOS is this: is the egg computable? In other words, is there some computation that would enable us to predict the outcome of embryonic development? And if that were not possible, would it at least be feasible to simulate the whole process and so arrive at the outcome? Such a simulation might require the behaviour of every cell to be modelled. If so, how much detail in each cell needs to be included? And how 'sharply' must the initial conditions be defined? I await the answer with little optimism.

I am greedy. I want to ask one other question. How is the left–right asymmetry of the embryo set up? We think it is based on an asymmetric molecule that becomes aligned with respect to the anteroposterior and dorsoventral axes and then provides a left–right bias [2]. Are we right?

References

1. Wolpert L: **Do we understand development?** *Science* 1994, **266**:571–572.
2. Brown NA, Wolpert L: **The development of handedness in left/right asymmetry.** *Development* 1990, **109**:1–9.

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The editors of *Current Biology* have invited a number of eminent biologists to respond to this article by Lewis Wolpert with brief essays which will be published in future issues. If you have any comments or ideas arising from this or the subsequent essays, we shall be happy to consider them.

Correspondence

Graduate school: the board game

William Wells

Cori Bargmann suggests depicting graduate school in a movie (*Current Biology* **5**:695), but as an outgoing graduate student, I envision it as a new and exciting board game.

'The Ego Game' starts with each player on 100 ego points. Anyone who gets to the finishing square (the 'OK, we'll give you a PhD' square) with five or more ego points intact is deemed a winner. Points are deducted along the way for lack of enthusiasm in the face of drudgery, grumbling about lack of future job opportunities in academia and expressing any desire to get reasonable health care out of a Student Health Service.

The danger really lies in the 'kick them while they are down' squares. Landing on one of these, the student must draw a card to determine his or her fate: persevere with idea independent from supervisor — lose 20 points; have vain hope that project will work — lose 10 points (if inside 12 months, lose 30 points); believe amount of effort plus amount of intelligence translates to amount of success — lose 50 points.

Landing on a 'good scientist' square gives you a 'blind luck' card. These cards give you the right to buy papers: a total of eight cards gives you a *Cell*, *Science* or *Nature* paper (and 50 ego points); four cards a *Journal of Cell Biology* paper; and two cards a *PNAS* paper (although if you pick up an 'influential professor' card the latter comes for free). Landing on the 'voracious young professor' square gets you four cards towards a paper, but minus 75 ego points. A 'holiday or alternative interest' square means that one paper card is taken away, but wins 30 'grip on reality' points which can be used to

advance towards the finish, 10 points per square. If you reach the end with fewer than two papers, you must have 60 ego points in reserve to buy a 'bowing and scraping to faculty' card.

I haven't integrated the 'genuine interest in science' card yet — I'm not sure where it fits. Maybe it will make the next version of the game. I hope to have this one out by next Christmas.

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Unit precedent

Brian Charlesworth

Sydney Brenner [1] suggests the use in evolutionary biology of the unit 'darwin' for 1 million years. In fact, the term darwin was introduced by Haldane in 1949 [2] for a change in a trait in an evolving lineage of e per million years (that is, a unit change per million years on a natural logarithm scale). As shown by Haldane [2] and by Simpson [3], rates of change in evolving fossil lineages are generally of the order of a few millidarwins.

References

1. Brenner S: **Molecular biology by numbers ... one.** *Curr Biol* 1995, **5**:964.
2. Haldane JBS: **Suggestions as to quantitative measurement of rates of evolution.** *Evolution* 1949, **3**:51–56.
3. Simpson GL: *The Major Features of Evolution.* New York: Columbia University Press; 1953.

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The editors of *Current Biology* welcome correspondence on any article in the journal, but reserve the right to reduce the length of any letter to be published. Items for publication should either be submitted typed, double-spaced, or sent by electronic mail. They should include a full contact address, with phone and fax numbers.

Gazetteer

Keystone symposia

What are they famous for? Providing relatively cheap ski vacations disguised as scientific meetings. Because the list of speakers is usually excellent, the disguise works reasonably well.

How did they start? Fred Fox of the University of California, Los Angeles (UCLA) organized the first meeting of what would become the UCLA Symposia, later the Keystone Symposia, at the Olympic Village in Squaw Valley in 1971.

When did they become dissociated from UCLA? In 1990, UCLA decided, for reasons that many found mysterious, that running the large organization that the UCLA Symposia had by then become was not a good use of their time; the Keystone Center, influenced by their Board of Trustees, some of whom were also sponsors of the symposia, agreed to take them on. The Keystone Symposia are currently in the throes of an amicable divorce from the Keystone Center; they will become independent, and retain the name.

What is the format of the meetings? The standard format consists of a morning plenary session (8–11 am), a poster session (usually 4–6 pm) and an evening plenary session (8–11 pm). The time from 11 am to 4 pm is free, and in most locations most people spend it skiing. Many people don't have the constitution required to stay awake in the evening session after an energetic afternoon's skiing, a few beers at the poster session, and a hurried dinner all on a short night's sleep at high altitude, however. The people chairing the sessions don't have much ability to modify the format of the meeting, although the Keystone Symposia organization says it will consider changes if there's a good enough reason for them.

Are all the meetings ski meetings? Not quite. For the last couple of years, Hilton Head Island has been used as a Keystone Symposia venue. It's about as far from the slopes as you can get without being in a desert. But the format is the same, and if you don't play golf take lots of work to fill your time.

How are the topics decided? An advisory board meets every September to discuss the proposals that have been sent in in the previous year. A typical proposal packet is about 6–7 pages long, and gives the goals of the meeting, a preliminary program, and an assessment of how many people might come. The proposals may also be 'refereed' by scientists in the area who are not part of the organizing group.

Who's on the advisory board? About 45 scientists from all walks of life, some of whom were invited to join, but some of whom simply volunteered to get involved.

Are they run for profit? No. The Keystone Center is a non-profit organization, and the new Keystone Symposia organization will be one too. Contributions from other organizations are therefore tax-deductible, and industrial sponsorship takes care of about 1/3 of the funding needed to subsidize academic speakers. Speakers from companies are generally asked to pay their own way.